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Modern Sedation and Analgesia Strategies in Neurocritical Care

Andrew Bauerschmidt[1,2] · Tarik Al-Bermani[3] · Syed Ali[1] · Brittany Bass[3] · Jessica Dorilio[1] · Jon Rosenberg[1,2] · Fawaz Al-Mufti[1,2]

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Abstract

Purpose of Review Patients with acute neurologic injury require a specialized approach to critical care, particularly with regard to sedation and analgesia. This article reviews the most recent advances in methodology, pharmacology, and best practices of sedation and analgesia for the neurocritical care population.

Recent Findings In addition to established agents such as propofol and midazolam, dexmedetomidine and ketamine are two sedative agents that play an increasingly central role, as they have a favorable side effect profile on cerebral hemodynamics and rapid offset can facilitate repeated neurologic exams. Recent evidence suggests that dexmedetomidine is also an effective component when managing delirium. Combined analgo-sedation with low doses of short-acting opiates is a preferred sedation strategy to facilitate neurologic exams as well as patient-ventilator synchrony.

Summary Optimal care for patients in the neurocritical care population requires an adaptation of general ICU strategies that incorporates understanding of neurophysiology and the need for close neuromonitoring. Recent data continues to improve care tailored to this population.

Keywords Neurocritical care · Sedation · Analgo-sedation · Pupillary reflex · Cerebral blood flow

Introduction

Achieving appropriate sedation and analgesia in the neurocritical care population is centered on balancing the need for close neurologic monitoring with the need for patient comfort and optimal long-term outcomes. The practice patterns and utilization of various sedative agents in the critically ill patient have been rapidly evolving over the past several years with some trends emerging, for example, the emergence of dexmedetomidine and ketamine as major sedative agents compared to older agents. This review first summarizes the properties of individual agents while noting particular properties of interest to the neurocritical care population and then highlights recent studies regarding evidence-based practices and overall approach.

✉ Andrew Bauerschmidt
Andrew.Bauerschmidt@wmchealth.org

[1] Department of Neurology-Westchester Medical Center, New York Medical College, Valhalla, NY, USA

[2] Department of Neurosurgery-Westchester Medical Center, New York Medical College, Valhalla, NY, USA

[3] Department of Pulmonary, Critical Care, and Sleep Medicine-Westchester Medical Center, Valhalla, NY, USA

Sedative Agents

Propofol

Propofol is an anesthetic that enhances the inhibitory effect of gamma-aminobutyric acid-A receptors [1]. It is one of the first-line sedatives to use in patients with elevated intracranial pressure (ICP) as it has a rapid onset of action ranging from 30 s to 2 min and can last up to 15 min, allowing for a physical exam assessment once sedation is turned off [2, 3, 4•]. Propofol is generally well tolerated and effectively reduces elevated ICP; however, it may lead to cerebral vasoconstriction and dose-dependent reduction in cerebral blood flow (CBF) and oxygenation, particularly when compared to sevoflurane and isoflurane [5, 6]. Further studies evaluating propofol using invasive brain monitoring showed that although propofol does reduce MAP and CPP, it simultaneously reduces the ICP resulting in reduced mortality rates in traumatic brain injury (TBI) patients [7]. Caution must

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be used when using propofol, as it can lead to systemic vasodilation and reduced inotropy causing a reduction in mean arterial pressure and impaired cerebral autoregulation. Additionally, patients may develop adverse effects including propofol infusion syndrome [1, 3].

Recent studies were aimed at looking at neurological outcomes in patients who are under general anesthesia vs conscious sedation during acute neurologic disease states. In 2017, the General Anesthesia versus Conscious Sedation for Endovascular Treatment of Acute Ischemic Stroke (AnSTROKE) trial that looked at 90 patients equally divided into general anesthesia versus conscious sedation during endovascular treatment for acute ischemic strokes revealed no significant difference in neurological outcomes 3 months after the stroke [8]. A subsequent study in 2018, Effect of General Anesthesia and Conscious Sedation during Endovascular Therapy on Infarct Growth and Clinical Outcomes in Acute Ischemic Stroke (GOLIATH), was a single-center, randomized clinical trial that looked at infarct growth during endovascular therapy for acute ischemic strokes. One hundred twenty-eight patients were studied from 2015 to 2017, allocated 1:1 in general anesthesia vs conscious sedation. Conscious sedation used a fentanyl bolus followed by low-dose propofol infusion. The general anesthesia arm was sedated with remifentanil drip plus propofol infusion at a higher dose. The investigators found that the volume of infarct was not statistically significant between the general anesthesia versus conscious sedation groups; however, there was a significant difference in modified Rankin scale score in the general anesthesia over the conscious sedation group [9]. In 2019, a meta-analysis was performed to evaluate the results of the GOLIATH, AnSTROKE, and SIESTA trials to evaluate outcome at 3 months in patients who received conscious sedation versus general anesthesia during thrombectomy. In this meta-analysis, the authors concluded that general anesthesia was associated with less disability in 3 months [10]. Given these studies, there may be a slight benefit towards patients who are sedated more deeply for endovascular treatment of acute ischemic strokes; the mechanism of this benefit is unclear and may be attributable to differential reperfusion rates or direct cerebral metabolic effects of the sedatives themselves.

Dexmedetomidine

Dexmedetomidine is a centrally acting alpha-2 adrenergic receptor agonist [11]. It is useful as it has anesthetic, analgesic, and sedative properties, leading to decreased additional opioid and anesthetic use without causing respiratory depression [7, 12]. Given these properties, it is useful as a patient can remain awake for neurologic examination with low-to-moderate doses [13]. A study has shown that use of dexmedetomidine resulted in a decrease in agitation in TBI patients within 96 h of its use [14].

Dexmedetomidine has minimal effect on cerebral hemodynamics, including CBF and brain tissue perfusion; however, it may modestly reduce ICP, theorized by its mild cerebral vasoconstriction effects, reduction in cerebral blood volume (CBV), and reduction in cerebral metabolic rate [1, 15–17]. A recent study on critically ill patients with TBI suggests that dexmedetomidine may reduce ICP, as dexmedetomidine infusion was associated with reduced need for rescue hypertonic therapy in this patient population [18]. Dexmedetomidine may reduce ICP in part by blunting sympathetic and catecholamine surges seen in brain-injured patients. Caution must be used with dexmedetomidine as it commonly causes bradycardia and hypotension, which may lead to a clinically significant reduction in mean arterial pressure. A meta-analysis showed that the incidence of bradycardia is consistent when evaluating patients across multiple different intensive care units [19]. When compared to propofol, dexmedetomidine had a higher incidence of hypotension [11, 20, 21]. Overall, the sympatholytic benefit of dexmedetomidine should be weighed against a possible reduction in cerebral perfusion pressure from bradycardia and systemic hypotension.

When weaning from long-duration continuous dexmedetomidine infusion, patients may experience rebound effects including tachycardia, hypertension, and potential re-emergence of agitation. An emerging strategy to counter this is transitioning to clonidine, which is also a centrally acting α_2 agonist, however with a longer half-life, and can be administered enterally. Clonidine can be administered every 6–8 h enterally or via transdermal patch over the course of approximately 24 h, and early data suggests that this can be an effective strategy [22].

Benzodiazepines

Benzodiazepines (BZDs) are a class of sedatives that work by modulating GABA receptors in the central nervous system to decrease neuronal excitation and can reduce cerebral metabolism. The pharmacokinetics of BZDs differ depending on which BZD is used; in critical care medicine, the most widely used BZD is midazolam [23, 24]. Intravenous midazolam typically reaches peak concentration in less than 5 min and has a half-life of around 1.5–3.5 h [23]. A prospective study in 2019 evaluating 96 patients with severe head injury found that sedation with midazolam controlled ICP in over two-thirds of patients with severe TBI [25]. Overall, however, BZDs are less preferred to other agents for both ICP control and sedation in general due to its association with longer duration of mechanical ventilation and ICU stay and higher rates of delirium [25–27]. BZDs may be preferred for sedation over other agents like propofol when

there are specific concerns about hemodynamic stability propofol infusion syndrome [25].

Ketamine

Ketamine acts primarily as an NMDA receptor antagonist, diminishing the excitatory effects of glutamate at these receptors. Ketamine also has activity on muscarinic, nicotinic, and opioid mu-receptors. Previously, ketamine was avoided in patients with acute brain injury as it was thought to increase ICP through sympathetic stimulation [28]. However, more recent studies in patients with acute brain injury have shown that high-dose ketamine provides both sedative and analgesic properties while maintaining constant mean arterial, cerebral perfusion, and ICP and in some cases reducing ICP [7, 29, 30]. Ketamine may play a role in neuroprotection though several mechanisms, including reducing microglial activation, excitotoxicity, and cortical spreading depolarization [31]. Ketamine can induce both sedation and analgesia at high doses without reducing mean arterial pressure and thus may be an ideal medication in patients with acute brain injury.

A recently emerging strategy for conscious procedural sedation is to combine ketamine and propofol ("ketofol") to create a synergistic sedation state. Multiple small prospective trials have studied this combination, suggesting that it may create a more stable procedural sedation state and be well tolerated [32, 33]. Other studies have suggested that there is no clear clinical benefit over propofol alone and may be higher rates of hypotension and other adverse effects [34]. No conclusions about benefits/risks can be drawn with the current level of evidence, and additional studies are warranted to see if this strategy can specifically benefit the neurocritical care population.

Barbiturates

Barbiturates are not first-line agents for general sedation, but are utilized as an effective agent for treating refractory elevated intracranial pressure. Barbiturates act by increasing the duration of chloride channel opening which enhances GABA-induced postsynaptic inhibition [35]. The pharmacokinetics differ based on the agent used, with ultra-short-acting agents having onsets of 2–4 min and long-acting agents such as phenobarbital having slower onset of action [36]. In patients with refractory intracranial hypertension, secondary medical therapy includes use of barbiturates (typically phenobarbital or pentobarbital) to dramatically reduce cerebral metabolism by inducing coma [37]. One randomized multi-center trial demonstrated that institution of barbiturate coma in patients with refractory ICP crises led to a twofold greater chance of controlling ICP [38]. The mechanisms by which ICP is reduced are due to reducing CBF, reducing cerebral oxygen consumption and metabolism, and decreasing neuro-excitotoxicity via reduction of brain glutamate and aspartate release [37, 39]. One small study published in 2021 evaluated a novel step-down infusion method of barbiturate therapy which showed promising results for safety and efficacy of utilizing barbiturates for reduction of ICP though results are limited [40].

Barbiturates must be used with caution as they may lead to reduction in cardiac function as well as severe acute hypokalemia [40]. The half-life of long-acting barbiturates like phenobarbital can be 24–96 h, and with prolonged use of medium-acting pentobarbital infusions, elimination may also be severely delayed with half-life 20–45 h making neurologic exams difficult in these patients for a protracted period of time [36].

Opioids

Most critically ill patients benefit from a combination of analgesia and sedation ("analgo-sedation") depending on factors such as the presence of interventions that may be painful or uncomfortable, presence of brain injury, and degree of ventilator synchrony. Pain should be frequently and objectively assessed, using a validated pain scale, such as the Critical Care Pain Observation Tool (CPOT) or Behavioral Pain Scale (BPS); however, there is currently no pain scale specifically tailored to patients with neurologic injury, and difficulties in communication or physical expression of pain must be accounted for on an individual basis [41].

Opioids are the mainstay of analgesia in many ICU populations, particularly for patients with an endotracheal tube in place, as it may induce the cough reflex or discomfort from direct tracheal stimulation. In one large prospective multicenter trial, opioid use resulted in lower ventilator asynchrony compared to sedation alone [42•]. Fentanyl and remifentanil are commonly preferred opioids as they have short time to onset of effect (< 5 min) and short half-lives, approximately 2 h and 10 min, respectively. Morphine and hydromorphone are also utilized; however, their longer half-lives may prohibit frequent neurologic exams if used at higher doses for longer periods and may prolong ventilator time [43]. Treatment of pain should take a multi-modal approach in which moderate doses of agents from both opioid and non-opioid classes are utilized together with the aim of both avoiding toxicity and creating synergistic analgesia. Typical non-opioid pharmacologic agents include NSAIDs, acetaminophen, ketamine, and neuropathic pain agents, among others [44].

In contrast to all GABA agonists which reduce cerebral metabolic demand ($CRMO_2$) and consequently reduce CBF and CBV, a systematic review of patients with TBI suggests that opioid infusions generally have little effect on cerebral

hemodynamics; however, bolus dosing may result in decreased MAP and concomitant decrease in CPP [45]. Of note, morphine and hydromorphone should be used in caution in patients with acute brain injury and renal impairment as their metabolites (morphine-3-glucuronide and hydromorphone-3-glucuronide) have been linked to neurotoxicity, including seizures, tremors, and myoclonus, particularly when used in high doses and for prolonged duration [46].

Neuromuscular Blockers

Neuromuscular blockers (paralytics) are not sedation agents; however, they are often used in conjunction with sedatives and have special considerations in the neurocritical care population. Use for intubation, ventilator compliance, refractory ICP control, or other indications is common in the neurocritical care unit. Neuromuscular blockage is used to treat refractory ICP crises; however, there is no high-quality evidence supporting this practice [47]. Paralytics commonly used in rapid sequence intubation are divided into depolarizing and non-depolarizing agents. The only widely used depolarizing agent is succinylcholine, which acts by binding to and activating the post-synaptic acetylcholine receptor causing repeated muscle fasciculations for approximately 30 s prior to paralysis. Rapid onset and offset make it one of the favorable medications used in intubation, especially in the neuro-ICU, where rapid return of a neurologic exam is valued [48].

There are numerous reported adverse effects with succinylcholine, including hypersensitivity, malignant hyperthermia, and transient increase in potassium, some of which are particularly common in the neurologic population. Conditions such as stroke with paralysis, spinal cord injury, demyelinating disorders, and prolonged immobility in patients can result in compensatory increases in nicotinic acetylcholine receptors in weak musculature; succinylcholine use in these patients can lead to prolonged paralysis and non-depolarizing agents are preferred [49]. Succinylcholine is specifically contraindicated in Guillain–Barre syndrome as multiple case reports show that it may cause life-threatening hyperkalemia [50–52]. Previous theories hypothesized that the muscle fasciculations induced from depolarization may cause a transient rise in ICP; however, a meta-analysis conducted failed to show such an association although evidence is weak [53]. All ICU patients are vulnerable to critical illness neuropathy and myopathy, and this risk is likely exacerbated in patients with primary neuromuscular diseases.

Integrated Approach to Sedation

In the context of neurocritical care, there is a need for consistent monitoring of neurologic functioning, and the clinical neurologic exam or "neurological wake up test" (NWT) remains the gold standard for examining patients with acute brain injury. Dexmedetomidine and propofol are most frequently used to achieve rapid awakening allowing for consistent NWTs, and lighter rather than deep sedation also facilitates this goal [54, 55]. Recent data has encouraged a shift towards the preferential use of dexmedetomidine compared to primary use of propofol, midazolam, and fentanyl among other commonly used agents. According to a recent open-labeled, randomized clinical trial involving 4000 patients in the *New England Journal of Medicine*, dexmedetomidine as the sole or primary sedative can consistently provide lighter levels of sedation as measured by the Richmond Agitation and Sedation Scale (RASS) in the target range of − 2 (light sedation) to + 1 (restless) compared to propofol, midazolam, or other sedatives [56].

Directly comparing two of these agents, a recent study published in the *Journal of Critical Care* found that dexmedetomidine was used more commonly for facilitating extubation, alcohol withdrawal, and sedation during frequent neurologic assessments [57]. The same study also found that there was no difference in duration of infusion, lengths of stay, duration of mechanical ventilation, rates of hypotension, nor rates of bradycardia with the use of dexmedetomidine versus propofol [57]. Dexmedetomidine reduces the latency to target sedation range and increases time under light sedation compared to midazolam and propofol [58–60]. In addition, to prolong the duration of light sedation, dexmedetomidine may be supplemented with midazolam or propofol [56]. Patient comfort must also be considered whenever conscious sedation is required. Patient comfort scores are comparable with dexmedetomidine and midazolam sedation [61].

Another method which is frequently utilized by clinicians to prolong light sedation is to combine intravenous as-needed pushes of fentanyl in conjunction with continuous dexmedetomidine infusion. However, an emerging and ameliorated strategy compared to using fentanyl with dexmedetomidine is to utilize remifentanil, an ultra-short-acting opioid, with dexmedetomidine. In one recent study, remifentanil elicited a deeper analgesic state without accumulating in tissues significantly and increased the proportion of time under light sedation compared to fentanyl with dexmedetomidine in adults receiving mechanical ventilation (MV) in the intensive care unit [62]. Remifentanil offers more consistent maintenance of light sedation for a greater duration compared to fentanyl when added to dexmedetomidine [62]. Another strategy is to pre-treat with minor doses of dexmedetomidine (0.5 μg/kg or 1 μg/kg), which has been shown to increase the instances of conscious sedation and reduce the requirement of propofol, conferring protection against oversedation [58].

Dexmedetomidine is a generally preferred agent (primary or adjunctive) for frequent neurological exams and

procedural and light sedation, while propofol may still be more effective for deeper sedation needs. In a study of post-surgical patients who suffered intracerebral hemorrhage, no significant differences existed in the time to achieve target sedation between dexmedetomidine and midazolam, but dexmedetomidine was associated with better patient prognosis and lower levels of agitation [63]. In one study of patients with TBI, patients receiving dexmedetomidine experienced higher levels of agitation and required additional sedatives as compared to propofol [59]. Other studies have shown it to be a safe alternative to propofol and equally effective in reducing agitation after TBI [64]. Thus, there remains a need for additional research regarding this mixed data and which agents may be ideal for different acute brain injury populations as compared to the general ICU population.

Patient ventilator asynchrony (PVA) is a complication associated with worse prognosis in critically ill patients that is described as a mismatch between patient-triggered breaths and breaths delivered by a mechanical ventilator [65, 66]. Patients with neurological insults are especially susceptible to PVA due to involvement of respiratory centers in the brain, with the predominant form of PVA being ineffective triggering of breaths [66]. Lighter levels of sedation provided by dexmedetomidine allow for patient control of breathing, fewer ineffective breaths, and reduced PVA, while fentanyl with midazolam is associated with worsening of PVA, possibly due to the deeper level of sedation provided by this combination [65, 66]. Opioids (morphine or fentanyl) used alone are associated with decreased levels of asynchrony, leading to better outcomes and preserved consciousness [42•]. In mechanically ventilated children with TBI, a continuous infusion of remifentanil provides target sedation while allowing for ease of awakening to facilitate reproducible neurological examinations [67]. Taken together, opioids and dexmedetomidine show promise with balancing patient-ventilator asynchrony, while allowing for frequent neurological exams. However, these conclusions must be interpreted with caution as more research with diverse neurological pathologies and larger sample sizes must be conducted to ensure reproducibility of these results.

While there exist numerous studies exploring the efficacy of sedatives in terms of maintaining wakefulness and constant neurological monitoring during surgical procedures such as craniotomies and implantations, there is limited updated literature with regard to examining the utility of these drugs specifically in the neurocritical care unit setting specifically to facilitate optimized neuromonitoring. The general approach at this time is to use a non-opioid strategy or a combination of short-acting opioids with other agents to achieve to greater duration of light sedation. Furthermore, in some patients with depressed levels of consciousness due to acute brain injury, an adequate RASS level as well as adequate ventilator synchrony may be achieved with little or no sedation at all and this may be an acceptable strategy to trial on a case-by-case basis.

Pharmacologic Effects on Pupillary Reflexes

In addition to cerebral hemodynamics, sedative and analgesic agents can directly influence the rudimentary neurological exam, particularly the pupillary reflex. Clinicians should be aware of how these medications influence the neurological exam when caring for patients with acute brain injury.

GABA agonist sedatives such as propofol, midazolam, and barbiturates can suppress brainstem reflexes, including pupillary reactivity [68–71]. However, the effect of GABA agonists on the pupillary reflex appears to be dose dependent, with increasing doses leading to greater reduction in pupillary size and pupillary reactivity [72, 73]. At sub-anesthetic doses, the effect of benzodiazepines on pupillary function is likely negligible [74]. However, studies have shown reduction in pupillary size and reactivity (as measured by quantitative pupillometry) in patients receiving high anesthetic doses to achieve deep sedation [70]. Taking this into consideration, the loss of pupil reactivity should not be attributed to moderate sedation with these agents at the risk of failing to identify a new neurologic decline.

Studies examining the effect of dexmedetomidine on pupillary function have shown mixed results. A large retrospective study of critically ill adults ($n = 221$) found that initiation of dexmedetomidine infusion was associated with reduced pupillary size and increased pupillary reactivity as measured by neurologic pupillary index on pupillometry testing [75]. A smaller single-center observational study also reported that dexmedetomidine improved pupillary reactivity on quantitative pupillometry testing, though it reported no effect on resting pupillary size [76].

Opioids cause miosis through central disinhibition of parasympathetic neurons in the Edinger-Westphal nucleus [77]. However, with the advent of quantitative pupillometry, studies have shown that pupillary constriction velocity and neurologic pupillary index remain preserved with high-dose opioid infusions, even when the absolute size is reduced [78, 79].

There are few studies examining the effect of ketamine and other NMDA antagonists on pupillary function, and the literature is limited to small single-center studies and case reports. In these studies, ketamine infusion (at general anesthetic doses) reduced pupillary size and reactivity on quantitative pupillometry [80, 81]. These findings are likely explained by ketamine's cross-reactivity with muscarinic receptors.

Unlike sedative and analgesic agents, neuromuscular paralytic agents do not alter pupillary light reflex, as they target nicotinic receptors of the somatic nervous system, as opposed to parasympathetic and sympathetic neurons that

influence pupillary function. This finding was demonstrated in a large randomized clinical trial, which showed that various paralytic agents had no significant effect on the pupillary light reflex [82].

Delirium in Neuro-intensive Care Units

Delirium is an acute, fluctuating, yet reversible deterioration in neurocognitive function and attention which may be associated with both agitation and hypoactivity. It is commonly associated with the use of sedation and analgesic agents, but also frequently treated with sedatives or antipsychotics. In the critical illness population, the most widely used method for diagnosing and assessing delirium is the Confusion Assessment Method for the intensive care unit (CAM-ICU) [83]. However, in patients with acute brain injury, particularly those with stroke and language impairment, this score may not be as effective for diagnosis as it depends on intact language comprehension [84]. In patients who have impaired language, the use of the Intensive Care Delirium Screening Checklist, or a fluctuating Richmond Agitation and Sedation Scale (RASS), may be more useful indicators of delirium [85, 86]. Patients with neurologic injury may be incorrectly diagnosed with delirium, and caution should be taken when assessing features of delirium vs that of the underlying injury [87].

Delirium is a particularly challenging complication faced frequently by clinicians in the critically ill patients. It also poses a great medical burden by prolonging hospital stay, duration of mechanical ventilation, and increasing morbidity and mortality [88]. Important risk factors that predispose patients to delirium are polypharmacy in elderly patients with pre-existing co-morbidities and those who suffer from multiple organ failures [88]. Combinations of loop diuretics, benzodiazepines, antipsychotics, and medications with anticholinergic properties greatly increase delirium risk [88–91]. In addition, the H_2 antagonists and PPIs for gastric stress ulcer prophylaxis in ICU patients have also been implicated in delirium [92].

Haloperidol and other typical antipsychotics have long been used to treat agitation in the context of delirium. According to a recent prospective cohort study published in the *Journal of Intensive Care*, investigating 3614 mixed ICU patients, the use of haloperidol in critically ill patients as prophylaxis or abortive therapy is associated with poor outcomes compared to untreated delirious patients [91]. In fact, it should be noted that combining haloperidol with clonidine or benzodiazepines (lorazepam) increases duration of delirium, lowers the odds of resolution, and prolongs ICU stay compared to patients untreated for delirium [90, 91]. In a subset of post-operative ICU patients, haloperidol did reduce the incidence of delirium [93]. While haloperidol is associated with negative outcomes regarding delirium [90, 91], multiple smaller studies suggest that prophylactic use of second-generation antipsychotics may decrease agitation, reduce the incidence of delirium, and shorten duration of delirium episodes without the adverse EPS and QTc prolongation effects [94–96]. Most similar pharmacologic trials have focused on patients with delirium and agitation, given the sedative effects of all antipsychotics. In a large placebo-controlled trial of both haloperidol and ziprasidone for delirium, no benefit was observed; however, this study included use of antipsychotics to patients with hypoactive delirium which is an uncommon practice and therefore may not be a generalizable result [97]. More studies must be conducted to clarify the relationship of antipsychotics with delirium and ideally independently assess hyperactive and hypoactive delirium subsets as they are typically identified and treated differently in clinical practice.

Multiple recent studies have provided evidence with regard to the overall approach to pharmacological management of delirium in ICU patients. There is a growing preference to use dexmedetomidine as it reduces patient agitation and lowers the incidence of delirium compared to those treated with haloperidol or propofol [98, 99]. Antiseizure medications like valproic acid in conjunction with benzodiazepines, opioid therapy, and antipsychotics show a daily downward trend in the prevalence of delirium and agitation, while monotherapy results in significant delirium improvement [100, 101]. Altogether, a variety of pharmacologic options are available; however, more controlled studies with these medications in ICU subpopulations must be conducted to tailor treatments and allow for better prognosis. It is also well established that non-pharmacologic strategies are effective in both preventing and treating delirium in the high-risk ICU population, including daily spontaneous awakening trials, early mobilization, restraint removal, bright light therapy, and frequent reorientation [102, 103].

Conclusions

The current approach to sedation and analgesia in the neurocritical care population is advancing by adapting generalized data from all-comer ICU populations and tailoring it specifically based on an understanding of neurophysiology and the specific needs of these patients. The primary goal remains achieving adequate sedation for ventilated patients or needed procedures, while facilitating close neuromonitoring and not disrupting cerebral hemodynamics. Careful drug selection and active monitoring and adjustment of sedatives are key to attaining these goals.

Declarations

Conflict of Interest The authors have no relevant funding sources nor conflicts of interest to report.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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